

Claims:

1. A DNAzyme which specifically cleaves RelA(p65) mRNA, the DNAzyme comprising

5 (i) a catalytic domain which cleaves mRNA at a purine:pyrimidine cleavage site;

(ii) a first binding domain contiguous with the 5' end of the catalytic domain; and

(iii) a second binding domain contiguous with the 3' end 10 of the catalytic domain,

wherein the binding domains are sufficiently complementary to the two regions immediately flanking a purine:pyrimidine cleavage site within the region of RelA(p65) mRNA corresponding to nucleotides 1 to 1767 as 15 shown in SEQ ID NO:1, such that the DNAzyme cleaves the RelA(p65) mRNA.

2. A DNAzyme as claimed in claim 1 wherein each binding domain is nine or more nucleotides in length.

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3. A DNAzyme as claimed in claim 1 or claim 2 in which the catalytic domain has the nucleotide sequence GGCTAGCTACAACGA (SEQ ID NO: 2).

25 4. A DNAzyme as claimed in any one of claims 1 to 3 in which the cleavage site corresponds to a site selected from the group consisting of:

(i) the AT site at nucleotides 80-81;

(ii) the GT site at nucleotides 91-92;

30 (iii) the GT site at nucleotides 140-141;

(iv) the AT site at nucleotides 149-150;

(v) the AT site at nucleotides 215-216;

(vi) the AT site at nucleotides 237-238;

(vii) the AT site at nucleotides 260-261;
(viii) the GT site at nucleotides 350-351;
(ix) the GT site at nucleotides 438-439;
(x) the AT site at nucleotides 479-480;
5 (xi) the GT site at nucleotides 525-526;
(xii) the GT site at nucleotides 572-572;
(xiii) the AT site at nucleotides 583-584;
(xiv) the GT site at nucleotides 726-727;
(xv) the GT site at nucleotides 734-735;
10 (xvi) the AT site at nucleotides 749-750;
(xvii) the AT site at nucleotides 807-808;
(xviii) the GT site at nucleotides 830-831;
(xix) the AT site at nucleotides 951-952;
(xx) the GT site at nucleotides 963-964;
15 (xxi) the AT site at nucleotides 1070-1071;
(xxii) the GT site at nucleotides 1076-1077;
(xxiii) the GT site at nucleotides 1100-1101;
(xxiv) the AT site at nucleotides 1125-1126;
(xxv) the AT site at nucleotides 1175-1176;
20 (xxvi) the GT site at nucleotides 1235-1236;
(xxvii) the AT site at nucleotides 1279-1280;
(xxviii) the GT site at nucleotides 1307-1308;
(xxix) the GT site at nucleotides 1313-1314;
(xxx) the GT site at nucleotides 1387-1388;
25 (xxxi) the AT site at nucleotides 1416-1417;
(xxxii) the GT site at nucleotides 1484-1485;
(xxxiii) the GT site at nucleotides 1529-1530;
(xxxiv) the AT site at nucleotides 1553-1554; and
(xxxv) the AT site at nucleotides 1697-1698.

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5. A DNAzyme as claimed in claim 4 in which the cleavage site corresponds to the GT site at nucleotides 91-92.

6. A DNAzyme as claimed in claim 1 which has a sequence selected from the group consisting of:

5' GTTCGTCCAGGCTAGCTACAAACGAGGCCGGGT 3' (SEQ ID NO:3);
5' GAGGGGAAAGGCTAGCTACAAACGAAGTTCGTCC 3' (SEQ ID NO:4);
5' TGATCTCCAGGCTAGCTACAAACGAATAGGGGCC 3' (SEQ ID NO:5);
5' GCTGCTCAAGGCTAGCTACAAACGAGATCTCCAC 3' (SEQ ID NO:6);
5' CGCCTGGGAGGCTAGCTACAAACGAGCTGCCGC 3' (SEQ ID NO:7);
5' TTGGTGGTAGGCTAGCTACAAACGACTGTGCTCC 3' (SEQ ID NO:8);
5' TGATCTTGAGGCTAGCTACAAACGAGGTGGGTG 3' (SEQ ID NO:9);
10 5' CCTTCCTAGGCTAGCTACAAACGAAAGCTCGTG 3' (SEQ ID NO:10);
5' TTCTTCACAGGCTAGCTACAAACGAACCTGGATT 3' (SEQ ID NO:11);
5' TGGTCTGGAGGCTAGCTACAAACGAGCGCTGACT 3' (SEQ ID NO:12);
5' TAGTCCCCAGGCTAGCTACAAACGAGCTGCTTT 3' (SEQ ID NO:13);
5' GGTCCCGCAGGCTAGCTACAAACGATGTCACCTG 3' (SEQ ID NO:14);
15 5' CCTGCCTGAGGCTAGCTACAAACGAGGGTCCC 3' (SEQ ID NO:15);
5' ACCTTGTCAAGGCTAGCTACAAACGAACAGTAGGA 3' (SEQ ID NO:16);
5' CTTTCTGCAGGCTAGCTACAAACGACTTGTCA 3' (SEQ ID NO:17);
5' ACACCTCAAGGCTAGCTACAAACGAGTCCTCTT 3' (SEQ ID NO:18);
5' CGGTGCACAGGCTAGCTACAAACGACAGCTTGCG 3' (SEQ ID NO:19);
20 5' TCCGGAACAGGCTAGCTACAAACGAAATGGCCAC 3' (SEQ ID NO:20);
5' TCGTCTGTAGGCTAGCTACAAACGACTGGCAGGT 3' (SEQ ID NO:21);
5' ATCCGGTGAGGCTAGCTACAAACGAGATCGTCTG 3' (SEQ ID NO:22);
5' GCACAGCAAGGCTAGCTACAAACGAGCGTCGAGG 3' (SEQ ID NO:23);
5' GGGAAAGGCAGGCTAGCTACAAACGAAGCAATGCG 3' (SEQ ID NO:24);
25 5' GCTTGGGAGGCTAGCTACAAACGAAGAAGCTGA 3' (SEQ ID NO:25);
5' GTAAAGGGAGGCTAGCTACAAACGAAGGGCTGGG 3' (SEQ ID NO:26);
5' GAAACACCAGGCTAGCTACAAACGAGGTGGGAAA 3' (SEQ ID NO:27);
5' GGGGCAGGAGGCTAGCTACAAACGATTGGGAGG 3' (SEQ ID NO:28);
5' CAGAGCTGAGGCTAGCTACAAACGAACCATGGCT 3' (SEQ ID NO:29);
30 5' GGAAGTGGAGGCTAGCTACAAACGAAGGGCTGG 3' (SEQ ID NO:30);
5' GGGCTAGGAGGCTAGCTACAAACGATGGGACAGG 3' (SEQ ID NO:31);
5' GCCCTCTGAGGCTAGCTACAAACGAAGCGTTCC 3' (SEQ ID NO:32);
5' TCTTCATCAGGCTAGCTACAAACGACAAACTGCA 3' (SEQ ID NO:33);

5' AGTTGTCGAGGCTAGCTACAAACGAGGATGCCAG 3' (SEQ ID NO:34);
5' GGGGGGCCAGGCTAGCTACAAACGAAGGTATGCC 3' (SEQ ID NO:35);
5' CCATCAGCAGGCTAGCTACAAACGAGGGCTCAGT 3' (SEQ ID NO:36);
and
5 5' AGAAGTCCAGGCTAGCTACAAACGAGTCCGCAAT 3' (SEQ ID NO:37).

7. A DNAzyme as claimed in claim 6 which has the sequence
5' GAGGGGGAAGGCTAGCTACAAACGAAGTTCGTCC 3'.

10 8. A DNAzyme as claimed in any one of claims 1 to 7,
wherein the 3'-end nucleotide residue is inverted in the
binding domain contiguous with the 3' end of the catalytic
domain.

15 9. A pharmaceutical composition comprising a DNAzyme
according to any one of claims 1 to 8 and a pharmaceutically
acceptable carrier.

20 10. A method of inhibiting NF- κ B activity in a cell which
method comprises introducing into the cell a DNAzyme of any
one of claims 1 to 8.

25 11. A method of inhibiting NF- κ B activity in a subject
which method comprises administering to the subject a
pharmaceutical composition of claim 9.

30 12. A method of treating an inflammatory disease in a
subject which method comprises administering to the subject
a therapeutically effective dose of a pharmaceutical
composition of claim 9.

13. A method as claimed in claim 12, wherein the inflammatory disease is selected from the group consisting of inflammatory arthritis, asthma, inflammatory bowel disease, septic shock and vasculitis.

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14. A method as claimed in claim 13, wherein the inflammatory arthritis is selected from the group consisting of rheumatoid arthritis, osteoarthritis and seronegative arthritis.

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15. A method of treating atherosclerosis in a subject which method comprises administering to the subject a therapeutically effective dose of a pharmaceutical composition of claim 9.

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16. A method of treating cancer or leukaemia in a subject which comprises administering to the subject a therapeutically effective dose of a pharmaceutical composition of claim 9.

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17. A method as claimed in any one of claims 10 to 15, wherein the method is performed *in vivo*.

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18. A method as claimed in any one of claims 10 to 15, wherein the method is performed *ex vivo*.